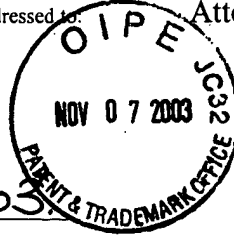


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PATENT
Attorney Docket No.: 020167-000130US

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Alexandria, VA 22313-1450



On November 5, 2003

TOWNSEND and TOWNSEND and CREW LLP

By: Marta Vanegas

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Zhong-Ru GAN

Application No.: 10/054,873

Filed: January 22, 2002

For: CHIMERIC PROTEIN
CONTAINING AN
INTRAMOLECULAR CHAPERONE-
LIKE SEQUENCE

Examiner: Not yet assigned

Art Unit: 1647

INFORMATION DISCLOSURE
STATEMENT UNDER 37 CFR §1.97 and
§1.98

Commissioner for Patents
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Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. In accordance with 37 CFR §1.98(d), copies of the references can be found in Application No. 09/423,100, filed December 11, 2000 (Attorney Docket No. 020167-000120US). It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.


As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

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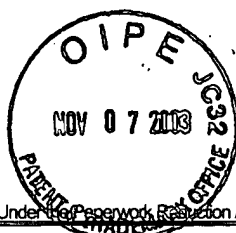
However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,


Frank J. Mycroft
Reg. No. 46,946

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
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Page 1 of 4

C m p l e i f K n w n

Application Number	10/054,873
Filing Date	January 22, 2002
First Named Inventor	Zhong-Ru Gan
Art Unit	1647
Examiner Name	Not yet assigned
Attorney Docket Number	020167-000130US

U.S. PATENT DOCUMENTS

Examiner	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number Kind Code ² (if known)			
	1	US-4,342,832	08/03/1982	Goeddel et al.	
	2	US-4,916,212	04/10/1990	Markussen et al.	
	3	US-5,254,463	10/19/1993	de Boer et al.	
	4	US-5,358,857	10/25/1994	Stengelin et al.	
	5	US-5,422,110	06/06/1995	Potter et al.	
	6	US-5,473,049	12/05/1995	Obermeier et al.	
	7	US-5,559,128	09/24/1996	Chakrabarty et al.	
	8	US-5,719,021	02/17/1998	Inouye	
	9	US-6,001,604	12/14/1999	Hartman et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³	Number ⁴	Kind Code ⁵ (if known)				
	10	EP	0 055 945	A2	07/14/1982	Genentech, Inc.		<input type="checkbox"/>
	11	EP	0 347 781	B1	02/16/1994	Hoechst Aktiengesellschaft		<input type="checkbox"/>
	12	EP	0 645 454	A2	03/29/1995	Lunin et al.		<input type="checkbox"/>
	13	WO	96/20724	A1	07/11/1996	Bio-Technology General Corp.		<input type="checkbox"/>
	14	WO	96/23888	A1	08/08/1996	G.D. Searle & Co.		<input type="checkbox"/>
	15	WO	97/18233	A1	05/22/1997	Pharmacia & Upjohn AB		<input type="checkbox"/>
	16	WO	02/079251	A2	10/10/2002	Novo Nordisk A/S		<input type="checkbox"/>

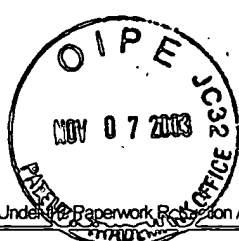
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Page 2 of 4

Complete if Known

Application Number	10/054,873
Filing Date	January 22, 2002
First Named Inventor	Gan, Zhong-Ru
Art Unit	1647
Examiner Name	Not yet assigned
Attorney Docket Number	020167-000130US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	17	BIOSIS DATABASE, Accession number 199497237023. Samuelsson <i>et al.</i> , 1994, "Enhanced <i>in vitro</i> refolding of insulin-like growth factor I using a solubilizing fusion partner," <i>Biochemistry</i> 33(14):4207-4211 (abstract)	
	18	BIOSIS DATABASE, Accession number PREV199799785120. Klappa <i>et al.</i> , 1997, "Interactions between protein disulphide isomerase and peptides," <i>European Journal of Biochemistry</i> 248(1):37-42 (abstract)	
	19	Bork and Bairoch, 1996, "Go hunting in sequence databases but watch out for the traps," <i>Trends Genet.</i> 12(10):425-427	
	20	Bork, P., 2000, "Powers and pitfalls in sequence analysis: the 70% hurdle," <i>Genome Res.</i> 10(4):398-400	
	21	Brenner, S.E., 1999, "Errors in genome annotation," <i>Trends Genet.</i> 15(4):132-133	
	22	Burgess, "Protein Purification," in <i>Protein Engineering</i> ; Oxender, D.L., Fox, C.F., Eds.; Alan R. Liss, Inc; NY, (1987), pp. 71-82.	
	23	Burnett, J. P., "Commercial Production of Recombinant DNA-Derived Products," in <i>Experimental Manipulation of Gene Expression</i> , Academic Press, NY, (1983), pp. 259-277.	
	24	Castellanos-Serra <i>et al.</i> , 1996, "Expression and folding of an interleukin-2-proinsulin fusion protein and its conversion into insulin by a single step enzymatic removal of the C-peptide and the N-terminal fused sequence," <i>FEBS Letters</i> , 378:171-176.	
	25	Chance <i>et al.</i> , "Chemical, Physical, and Biological Properties of Recombinant Human Insulin," in J. L. Gueriguian <i>Insulins, Growth Hormone, and Recombinant DNA Technology</i> , Raven Press, NY, (1981), pp. 71-85.	
	26	Chance <i>et al.</i> , "The Production of Human Insulin Using Recombinant DNA Technology and a New Chain Combination Procedure," in <i>Peptides: Synthesis-Structure-Function</i> , Pierce Chem. Co., Rockford, IL, (1981), pp. 721-728.	
	27	Diers <i>et al.</i> , "Yeast Fermentation Processes for Insulin Production," in Y. H. Chiu, <i>Drug Biotechnology Regulations: Scientific Basis and Practices</i> , Marcel Dekker, Inc., NY, (1991), pp. 166-176.	
	28	Doerks <i>et al.</i> , 1998, "Protein annotation: detective work for function prediction," <i>Trends Genet.</i> 14(6):248-250	
	29	Etienne-Decent, "Regulation of Protein Synthesis," in <i>Genetic Biochemistry: From Gene to Protein</i> , Ellis Horwood Limited, Chichester, U.K., (1988), pp. 125-127.	
	30	Frank and Chance, "The Preparation and characterization of human insulin of recombinant DNA origin," in <i>Therapeutic Agents Produced by Genetic Engineering "Quo Vadis?" Symposium</i> , (May 29-30, 1985), Sanoff Group, Toulouse-Labège, France, pp. 137-148.	

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STATEMENT BY APPLICANT**

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Page 3 of 4

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Applicant Number	10/054,873
Filing Date	January 22, 2002
First Named Inventor	Gan, Zhong-Ru
Art Unit	1647
Examiner Name	Not yet assigned
Attorney Docket Number	020167-000130US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	31	Frank and Chance, 1983, "Two Routes for Producing Human Insulin Utilizing Recombinant DNA Technology," <i>Munch. Med. Wschr.</i> 125(Suppl. 1):pp. S14-S20.	
	32	Goeddel <i>et al.</i> , 1979, "Expression in <i>Escherichia coli</i> of chemically synthesized genes for human insulin," <i>Proc. Natl. Acad. Sci. USA</i> 76(1): 106-110.	
	33	Ikehara <i>et al.</i> , 1984, "Synthesis of a gene for human growth hormone and its expression in <i>Escherichia coli</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 81:5956-5960.	
	34	Inouye, M., 1991, "Intramolecular Chaperone: The Role of the Pro-Peptide in Protein Folding," <i>Enzyme</i> 45:314-321.	
	35	Johnson, 1983, "Human Insulin from Recombinant DNA Technology," <i>Science</i> 219:632-637.	
	36	Johnson, R. D., 1986, "The Processing of Biomacromolecules: A Challenge for the Eighties," <i>Fluid Phase Equilib.</i> , 29:109-123.	
	37	Kroeff <i>et al.</i> , 1989, "Production Scale Purification of Biosynthetic Human Insulin by Reversed-Phase High-Performance Liquid Chromatography," <i>Journal of Chromatography</i> 461: 45-61.	
	38	Ladisch and Kohlmann, 1992, "Recombinant Human Insulin," <i>Biotechnol. Prog.</i> 8:469-478.	
	39	Ngo <i>et al.</i> , "Computational complexity, protein structure prediction, and the Levinthal Paradox," In: <i>The Protein Folding Problem and Tertiary Structure Prediction</i> , Merz and Le Grand, eds. Birkhauser, Boston, MA, 1994, pp. 433-506.	
	40	Norman and Litwack, "Pancreatic Hormones: Insulin and Glucagon," in <i>Hormones</i> , Academic Press, Inc., NY, (1987), pp 264-317.	
	41	Shinde and Inouye, 1993, "Intramolecular chaperones and protein folding," <i>TIBS</i> 18:442-446.	
	42	Skolnick and Fetrow, 2000, "From genes to protein structure and function: novel applications of computational approaches in the genomic era," <i>Trends Biotechnol.</i> 18(1):34-39	
	43	Smith and Zhang, 1997, "The challenges of genome sequence annotation or 'the devil is in the details,'" <i>Nat. Biotechnol.</i> 15(12):1222-1223	
	44	Thim <i>et al.</i> , 1986, "Secretion and processing of insulin precursors in yeast," <i>Proc. Natl. Acad. Sci. USA</i> 83:6766-6770.	

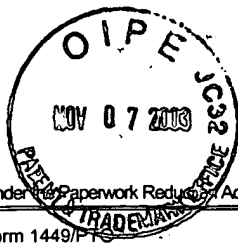
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Page 4 of 4

Compleat if Kn wn

Application Number	10/054,873
Filing Date	January 22, 2002
First Named Inventor	Gan, Zhong-Ru
Art Unit	1647
Examiner Name	Not yet assigned
Attorney Docket Number	020167-000130US

NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	45	Tottrup and Carlsen, 1990, "A Process for the Production of Human Proinsulin in <i>Saccharomyces cerevisiae</i> ," <i>Biotechnol. Bioeng.</i> 35:339-348.	
	46	Villa-Komaroff <i>et al.</i> , 1978, "A bacterial clone synthesizing proinsulin," <i>Proc. Natl. Acad. Sci. USA</i> 75(8):3727-3731.	
	47	Watson <i>et al.</i> , <i>Recombinant DNA—A Short Course</i> , Scientific American Books, W.H. Freeman Co., NY, (1983), pp. 231-241.	
	48	Wells, J. A., 1990, "Additivity of mutational effects in proteins," <i>Biochemistry</i> 29(37):8509-8517	
	49	Wheelwright, <i>Protein Purification: Design and Scale up of Downstream Processing</i> , Oxford University Press; NY, (1991), p.217.	
	50	Williams <i>et al.</i> , 1982, "Cytoplasmic Inclusion Bodies in <i>Escherichia coli</i> Producing Biosynthetic Human Insulin Proteins," <i>Science</i> 215:687-689.	

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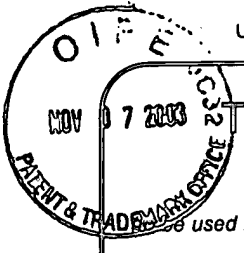
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		Filing Date	January 22, 2002
		First Named Inventor	Gan, Zhong-Ru
		Art Unit	1647
		Examiner Name	Not yet assigned
Total Number of Pages in This Submission		Attorney Docket Number	020167-000130US

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Firm or Individual	Townsend and Townsend and Crew LLP	
	Frank J. Mycroft	Reg. No. 46,946
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Date	November 5, 2003	

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